ClearH2O®

TECHNICAL BULLETIN

Pharmacokinetic determination of Carprofen and Meloxicam using the water gel formula **MediGel® Sucralose**

Introduction

Meloxicam and carprofen are two of most common drugs used for minor-mild pain procedures, indicated for perioperative analgesia and management of acute pain and chronic pain, in laboratory rodents. The most common route of administration for those medications is by injection. However, the process of injection itself produces some stress and discomfort to the animal due to the handling, restraint and pain due to the injection.

The purpose of this study was to determine whether a low-calorie thermoreversible water gel, **MediGel® Sucralose**, is a viable oral alternative to the traditional routes of administration (water bottles, injection, medicated diets, etc.) of liquid NSAID medications in laboratory rodents, and to determine whether the gel formulation is appropriate to achieve therapeutic levels. In addition to verifying efficacy, this study demonstrates that using a non-wetting sucralose flavored, low calorie water gel is a more ethical, painless alternative to injection, improving animal welfare. The research data revealed that therapeutic levels were achieved in mouse plasma for both AI (active ingredients), carprofen and meloxicam. These findings correspond well to rodent plasma concentration of these substances using traditional methods of administration (e.g. injections or per os administrations) , proving that drug administration using **MediGel® Sucralose** is a viable method in cases when animals should not be disturbed in their environment (e.g. germ-free programs, etc.).

Materials & Methods

Female C57BL6/J (n = 60; age, 8 wks.) mice were purchased from The Jackson Laboratories (Bar Harbor, ME). Mice were vendor-designated as SPF for all known mice pathogens and parasites. The mice were housed in ventilated cages in a controlled environment (T0C and H%) and were provided ad libitum food and water for the acclimation period. After acclimation, mice were randomly assigned into groups.

MediGel® Sucralose 2 oz cups (control or with medication) were added in to the animal cages during the acclimation period. The cage sippers were removed during the entire study period. Cups with **MediGel® Sucralose** were changed every second day.

MediGel® Sucralose cups were liquefied by heating in a water bath (PolySciences–ITM instruments) at 60°C for 15 minutes to ensure complete gel liquefaction. Drugs were mixed into cups liquid content for homogeneity, then covered and set in fridge until used. Cups were changed at every second day to avoid medicated **MediGel®** contamination with bedding and feces.

Drugs were obtained from CDMV (St-Hyacinthe , QC): RIMADYL: (Carprofen injectable solution 50 mg/ml), prod Zoetis Canada, Kirkland, QC, lot 1622016, exp 03/2021; METACAM: (Meloxicam, oral suspension 1.5 mg/ml), prod Boehringer Ingelheim, Burlington, ON, lot 859317, exp 12/2020. For each cup of 2oz (56g) of **MediGel® Sucralose**, the following dosage was used: Carprofen (50 mg/ml): 0.06 ml of stock solution; dose equivalent was 10 mg/kg; Metacam (1.5 mg/ml): 1.00 ml of stock solutions; dose equivalent was 5 mg/kg

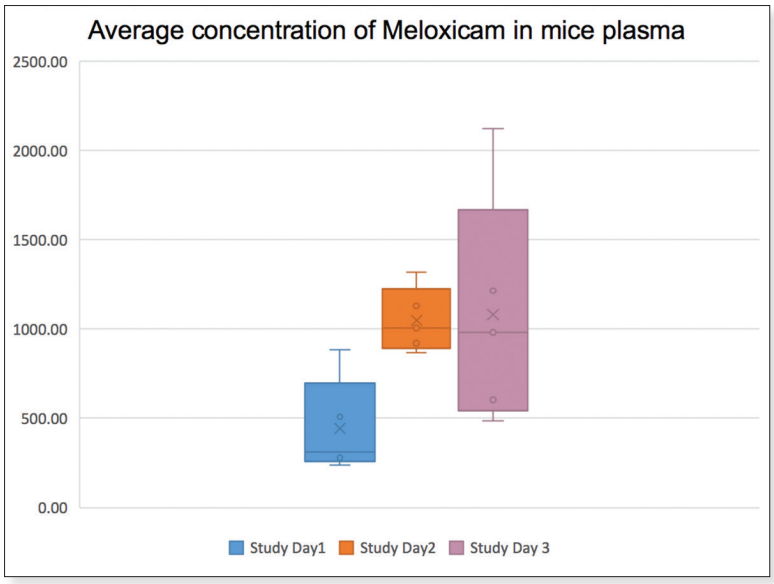
Five animals / group / time point were bled on Day 1 (72h after medication start), Day 2, Day 3, and Day 4. Control animals were also bled at each time point. All animals were monitored for dehydration signs. Body weight were measured at the beginning of the study and at each time point. All animals were clinically healthy throughout the study period.

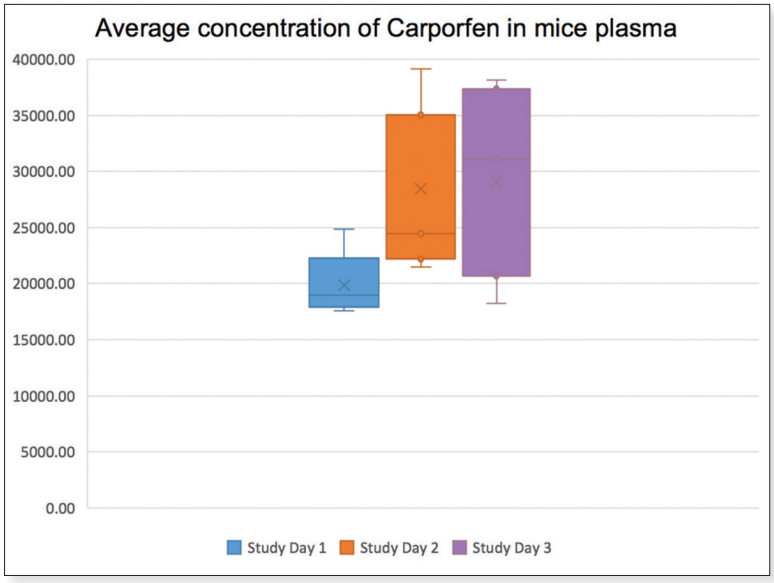
Each sample was tested twice and analyzed using a method that contains two different types of scans. The first method detected the protonated molecular ions four molecules and the second determination method detected an ionic fragment specific to each molecule.

Results & Discussion

Two of the most common non-steroidal anti-inflammatory drugs used for mild pain management in laboratory mice were administered using **MediGel® Sucralose** for four consecutive days. The graphs below show that the plasma concentrations of meloxicam and carprofen were very stable, increasing over time and reaching therapeutic levels when administered in **MediGel® Sucralose**. The variation in plasma levels isdue to individual animal consumption rate of the medicated **MediGel® Sucralose**; however, as noted above, the drug concentrations remain within therapeutic levels. The plasma concentrations of both drugs are comparable with the levels obtained when the drugs are administered by injection.

MediGel® Sucralose is an easy to use, convenient and effective method for administration of liquid medication including pain medication in laboratory mice. In order to achieve steady plasma concentrations and to provide the animals a steady source of hydration, **MediGel®** cups should be changed every two days.





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